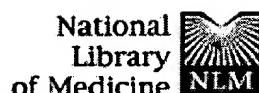


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Angiogenesis and tumor metastasis.

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Angiogenesis, the recruitment of new blood vessels, is an essential component of the metastatic pathway. These vessels provide the principal route by which tumor cells exit the primary tumor site and enter the circulation. For many tumors, the vascular density can provide a prognostic indicator of metastatic potential, with the highly vascular primary tumors having a higher incidence of metastasis than poorly vascular tumors. Tumor angiogenesis is regulated by the production of angiogenic stimulators including members of the fibroblast growth factor and vascular endothelial growth factor families. In addition, tumors may activate angiogenic inhibitors such as angiostatin and endostatin that can modulate angiogenesis both at the primary site and at downstream sites of metastasis. The potential use of these and other natural and synthetic angiogenic inhibitors as anticancer drugs is currently under intense investigation. Such agents may have reduced toxicity and be less likely to generate drug resistance than conventional cytotoxic drugs. Clinical trials are now underway to develop optimum treatment strategies for antiangiogenic agents.

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